

Appendix 1 (as provided by the authors): Detailed description of the Statistical analyses

We did an arm-based, random-effects model within an empirical Bayes framework using generalized linear mixed models (GLMM; i.e. a mixed effects logistic regression). We modelled the binary outcomes in every treatment group of every study, and specified the relations among the odds ratios (ORs) across studies making different comparisons. The GLMM models fit by the PROC GLIMMIX in SAS (SAS® 9.1.3, SAS Institute Inc, Cary, NC, USA) extend the general linear model by incorporating correlations among the responses. The class statement instructs the procedure to treat the variables drug, study, and the stratifying subgroups as classification variables. The model statement specifies the response variable as a sample proportion using an events/observations syntax; the procedure defaults to the binomial distribution. The denominator degrees of freedom for the tests of fixed effects resulting from the model were based on a general Satterthwaite approximation (ddfm=SATTERTH). A 'random statement' specifies that the linear predictor contains an intercept term that randomly varies at the level of the 'Study' as well as 'Study by Drug' interaction.

The indirect comparison (Δ) of each biologic to each other was done on the log-scale, thus $\Delta = \log(A) - \log(B) = \log(A/B)$ results in a modified Ratio of Odds Ratios (ROR) when back-transformed: $ROR = \exp(\log[A/B])$. The corresponding 95% Confidence Intervals were based on $\pm 1.96 \times SE(\log[A/B])$.